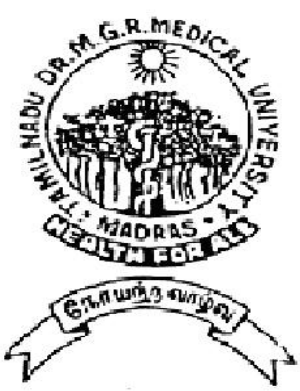
A STUDY OF SERUM ASCITES ALBUMIN GRADIENT IN THE ETIOLOGICAL DIAGNOSIS OF ASCITES



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CERTIFICATE

This is to certify that this dissertation entitled **'Serum Ascites Albumin Gradient in the Etiological Diagnosis of Ascites'** submitted by **Dr.Viji V. Julian** to the faculty of Medicine, The Tamil Nadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the requirement for the award of MD Degree Branch I (General Medicine), is a bonafide research work carried out by her under our direct supervision and guidance.

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CONTENTS

INTRODUCTION

Ascites is the pathological accumulation of fluid within the peritoneal cavity. It is one of the most common amongst the various clinical conditions, confronting not only a physician, but a surgeon and a gynaecologist too. It complicates a variety of disorders (1) which include cirrhosis, decompensated heart failure, nephrotic syndrome, peritoneal tuberculosis, disseminated carcinomatosis, pancreatitis, myxedema etc. In these conditions, ascites develops only as a consequence of the underlying illness. So the evaluation of the patients with ascites requires, that the cause of ascites be established. A proper diagnosis is a prerequisite for the successful management of these patients.

Diagnostic ascitic fluid aspiration is the most rapid and cost effective test for identifying the basic disease process. Before the 1980s, the ascitic fluid total protein [AFTP] concentration was used to classify ascites as either exudative [AFTP>/= 2.5 g/dl] or transudative [AFTP<2.5g/dl] (3).This classification is unable to correctly identify the etiological factors responsible for its causation. Hence this antiquated system of ascitic fluid classification is

problematic and it offers only a little insight to the pathophysiology of the ascitic fluid formation.

Further, these drawbacks led to the development of a new approach to classify ascites, based on the difference between the serum and ascitic fluid albumin concentration [Serum Ascites Albumin Gradient – SAAG] . This newer concept classified ascites into two categories – High SAAG ascites with SAAG >/= 1.1 g/dl in cases with portal hypertension and Low SAAG ascites with SAAG < 1.1 g/dl in cases with ascites, unrelated to portal hypertension.

The serum ascites albumin gradient has been proved in multiple studies to categorize ascites better than either the ascitic fluid total protein or other parameters in ascitic fluid analysis. In view of the above, the present study is undertaken among the inpatients, admitted with ascites in the medical wards of Tirunelveli Medical College Hospital, to evaluate the value of SAAG in the etiological diagnosis of ascites and also to compare its sensitivity and diagnostic accuracy with that of ascitic fluid total protein [AFTP].

AIM OF THE STUDY

1. To differentiate ascites on the basis of serum ascites albumin gradient into high SAAG ascites > 1.1 g/dl and low SAAG ascites < 1.1 g/dl.
2. To determine the sensitivity and specificity of serum ascites albumin gradient and that of ascitic fluid total protein, in identifying the etiology of ascites.
3. To compare the diagnostic accuracy of serum ascites albumin gradient with the traditional marker – ascitic fluid total protein.

REVIEW OF LITERATURE

Historical Perspective:-

Ascites is mentioned even in the most ancient of medical texts, i.e. the papyrus Ebers of Ancient Egypt and the ayurveda of Hindu tradition (Jalodara), both dating from as early as 1500-1600 BC [9]

The term "Ascites" first appeared in English in the late 14th century as Aschytes and was taken from the Greek word for dropsy 'askitos' [bladder, belly or bag], itself derived from an ancient Greek word for a leather bag or sheep skin, that was used for carrying water, wine, oil and so on.[9]

Anatomy of the Peritoneal Cavity:-

The peritoneal cavity is lined by the peritoneal membrane, that is composed of flattened polyhedral cells (mesothelium), one layer thick, resting upon a thin layer of fibroelastic tissue. Beneath the membrane, supported by a small amount of areolar tissue, lies a network of lymphatic vessels and rich plexuses of capillary blood vessels from which all absorption and exudation must occur. This membrane is a semipermeable one [7],[8].

The peritoneal membrane comprises of two components in continuity –

1. The visceral peritoneum covering the abdominal organs

2. The parietal peritoneum lining the abdominal wall.

The peritoneal cavity is thus a closed sac except for the fimbriated ends of the fallopian tubes and is the largest cavity in the body, with a total surface area of approximately 2 sq. m. In the normal healthy adult males, only a few ml of serous fluid is found in the peritoneal cavity, which provides a lubricant to allow the gliding movements of the viscera. Women may normally have as much as 20 ml of fluid, depending on the phase of the menstrual cycle [15].

P**athophysiology:-**

Ascites has fascinated doctors for many years and studies on its pathogenesis were initiated as long ago, as the seventeenth century. Richard Lower et al. (1631 – 1691), a physician, based in Oxford, demonstrated that ascites developed in dogs following ligation of inferior vena cava. Ernest Henry Starling et al. (1866 – 1927), a physiologist , based at University College, London made the greatest contribution to the study of oedema formation with the demonstration, that both lymphatic forces and oncotic forces were involved [5].

Starling's hypothesis: [12],[13]

The great British Physiologist E. H. Starling et al. in the early 20th century proposed the principle of movement of fluids from and to the capillaries. The primary forces that determine the fluid movement are termed Starling's forces in honour of him, who first demonstrated their importance. They are

1. The capillary pressure which tends to force fluid outward through the capillary membrane.
2. The interstitial fluid pressure which tends to force fluid inward through the capillary.
3. The capillary plasma colloid osmotic pressure which tends to cause osmosis of fluid inward through the capillary membrane.
4. The interstitial fluid colloid osmotic pressure which tends to cause osmosis of fluid outward through the capillary membrane.

This principle plays the major role in the pathogenesis of ascites.

Under normal conditions [10], the amount of peritoneal fluid is determined by a balance of intravascular forces, which attempt to push the fluid off (hydrostatic pressure) and to hold the fluid within (colloid osmotic pressure dependent mainly on serum albumin), the

vascular compartment. Ascites occurs when there is either an alteration[23] in the physiologic forces in the form of increased hydrostatic pressure (Portal hypertension, Constrictive pericardits, Decompensated Heart failure) or decreased serum albumin (nephrotic syndrome, cirrhosis, kwashiorkor) or primary diseases of peritoneum.[20]

Cirrhotic Ascites:[4],[27]

Theories regarding the mechanism of ascites formation [4]

All proposed mechanisms involve inappropriate renal sodium and water retention either secondary to vascular changes (Underfill theory and Peripheral arterial vasodilatation theory) or as a primary event (Overfill theory)

Sequence of events for the hypothesis of ascites formation:

Sequence	**Underfill & Peripheral vasodilatation theory**	**Overfill theory**
Primary	Vascular	Renal
Secondary	Renal	Vascular

Underfill Theory: [4]

The traditional underfill theory proposed that the inappropriate sequestration of fluid within the splanchnic vascular bed, which along with peripheral vasodilatation, associated with arteriovenous shunting led to a reduction in the central vascular compartment. The consequent decrease in effective circulating blood volume activates the renin angiotensin aldosterone system (RAAS) resulting in renal sodium and water retention.

Overfill hypothesis:

The overfill theory[4] suggests that, the primary abnormality is a defect in sodium handling. The proposal responsible for this is that, there is a primary renal change responding to a hepatic signal, that leads to sodium retention. The suggested signals are

a. Reduced hepatic synthesis of a natriuretic agent

b. Reduced hepatic clearance of a sodium retaining hormone

c. A Hepatorenal reflex of unknown etiology

The hypothesis proposed that the renal sodium and water retention leads to expansion of plasma volume, an increase in cardiac output and a fall in systemic vascular resistance.

Overfill theory:

Hepatic signal

↓

Renal sodium and water retention

↓

Increased Plasma volume , ↑ Cardiac output

↓ Systemic vascular resistance

↓

Portal hypertension

↓

Overflow into peritoneal cavity

Peripheral vasodilatation theory: (Schrier et al. 1988) [5],[4],[32]

The most recent theory is the Peripheral arterial Vasodilatation[4] hypothesis which is a modification of overfill theory. Nitric oxide is thought to play a central role. This leads to net arterial vasodilatation, reduced arterial vascular resistance, increased cardiac output and reduced filling of the central vascular compartment. Splanchnic arterial vasodilatation is accompanied by vasoconstriction in the renal, cerebral and muscular vascular beds. The renin angiotensin aldosterone system and sympathetic activity are

increased. The vasodilatation theory proposes that underfill is operative early and overfill is operative late in the natural history of cirrhosis.

Peripheral arterial vasodilatation hypothesis for ascites formation in cirrhosis [4]

Peripheral vasodilatation

↓

Diminished effective arterial bood volume

↓

Rise in Renin , Aldosterone, Vasopressin and Sympathetic stimulation

↓

Sodium and water retention, Renal vasoconstriction

↓

Plasma volume expansion + Portal hypertension

↓

Ascites

Vasodilators:

The factors responsible for splanchnic and arterial vasodilatation are not clearly understood. Endothelial cells may respond to changes in shear, stress, endotoxins or cytokines with the

production of vasodilators like nitric oxide. Nitric oxide synthesis is increased in cirrhotic patients. In an experimental model of cirrhosis, inhibition of nitric oxide synthase significantly reduced the plasma renin, aldosterone and vasopressin levels. Another new potent vasodilator – Adrenomedullin may also play a role. Other vasodilators that play a minimal role are Prostaglandins, Prostacyclin, atrial natriuretic peptide and calcitonin gene related peptide

Regardless of the initiating events, other factors like hypoalbuminemia and increased splanchnic and hepatic lymph formation contribute to the accumulation of fluid into the abdominal cavity in cirrhotic cases.

Noncirrhotic ascites :-

Cardiac ascites [3],[27]

Ascites can complicate high output or low output decompensated heart failure. As in cirrhosis, the effective arterial blood volume appears to be decreased and as a result the vasopressin, renin, aldosterone and sympathetic nervous systems are activated. These changes lead to renal vasoconstriction and sodium and water retention. Fluid then weeps from the congested hepatic sinusoids due to the increased sinusoidal pressure.

Malignant ascites [16],[35]

The mechanism of fluid retention in patients with malignancy related ascites depends on the location of the tumor and the ascites presents in one of four ways.

1. Peripheral ascites - Peritoneal carcinomatosis

It is the most common presentation and constitutes about 50% of cases. The mechanism of ascites formation in peritoneal carcinomatosis is through the production of proteinaceous fluid by the tumour cells lining the peritoneum. Extracellular fluid enters the peritoneal cavity to reestablish the oncotic pressure balance.

2. Central ascites:

It constitutes about 15% of cases. It can be due to either a primary hepatocellular carcinoma or a secondary metastatic deposit in the liver. In patients with hepatocelluar carcinoma, ascites arises because of the underlying cirrhosis – related portal hypertension, tumor induced portal vein thrombosis or both. Fluid accumulates in patients with massive liver metastases because of portal hypertension caused by stenosis or occlusion of the portal vein by tumor nodules or tumor emboli.

3.Mixed ascites:

It is due to the tumour deposits in the liver and the peritoneum

4.Chylous ascites:

It is due to the fluid accumulation from lymphatic invasion.

Tuberculous ascites: (3)

Tuberculosis probably causes ascites due to the production of proteinaceous fluid, as in peritoneal carcinomatosis.

Spontaneous bacterial peritonitis: (3),(24)

It dose not appear to cause fluid to accumulate. Infection develops only in preexisting ascites.

Pancreatic or Biliary ascites: (1),(3).

In patients with pancreatic or biliary ascites, fluid accumulates by leakage of pancreatic juice or bile into the peritoneal cavity, or from secondary to a 'chemical burn' of the peritoneum. The pancreatic fluid may extravasate from the pancreatic ductal system, most commonly from a leaking pseudocyst. After abdominal surgery especially extensive retroperitoneal dissection, lymphatics may be transected and may leak lymph for varying amounts of time.

Diagnosis :- [3],[33]

Although the diagnosis of ascites may be suspected on the basis of the history and physical examination, final confirmation is based on successful abdominal paracentesis and detection of ascites on imaging. Determination of the cause is based on history, physical examination, ascites fluid analysis and imaging studies.

In a patient presenting with ascites, for the first time, analysis of ascitic fluid should be done to determine the underlying etiology and and then confirmed by imaging techniques.

Ascitic fluid analysis [3]

The basic concept of ascitic fluid analysis is that the screening tests are performed on the initial specimen and additional testing is performed only when necessary as indicated by the results of the screening tests. On the basis of cost analysis, tests can be classified as routine, optional, unusual and unhelpful.

Routine	Optional	Unusual	Unhelpful
Cell count	Culture	TB Smear & Culture	Ph
Albumin	Glucose	Cytology	Lactate
Total protein	LDH	Triglyceride	Cholesterol
	Amylase	Bilirubin	Fibronectin
	Gram stain		Alpha1 Antitrypsin
			Glycosaminoglycans

The two tests highlighted in this study are ascitic fluid total protein and ascitic fluid albumin to detect SAAG.

Exudate / Transudate :-

Ascitic fluid total protein.

In the past, the ascitic fluid total protein concentration was used to classify ascites as either exudative (greater than 2.5 g/dl) or transudative (less than 2.5 g/dl).

Classification of ascites based on exudative / transudative[7]

I. Transudative ascites

A. Hypoalbuminemia

1. Nephrotic syndrome

2. Protein losing enteropathy

B. Venous hypertension

1. Due to high right sided cardiac pressure:

(i) Congestive heart failure

(ii) Tricuspid insufficiency

(iii) Constrictive Pericarditis

2. Blockage of Hepatic veins and / or Vena cava

(i) Hepatic vein blocks (Budd Chiari syndrome, webs, tumors)

(ii) Veno occlusive disease

C. Portal vein obstruction

D. Diffuse Parenchymal disease with portal hypertension – All forms of Cirrhosis

E. Infiltrative processes of the liver

1. Tumours, Lymphomas, Myeloid metaplasia

2. Granulomatous disease

II. Exudative ascites

A. Inflammatory diseases of the peritoneum

1. Tuberculosis

2. Bacterial Peritonitis

3. Pancreatitis

4. Rupture of viscus with / without an intraabdominal mass.

5. Bile peritonitis

B. Malignant causes

1. Metastases to liver or peritoneum

2. Primary hepatic tumours – Hepatocellular carcinoma, Cholangiocarcinoma

3. Primary Mesothelioma

C. Chylous ascites

1. Trauma to the thoracic duct

2. Mediastinal tumours

3. Filariasis

4. Tuberculosis

5. Cirrhosis (about 20% of patients)

The protein concentration in cirrhotic ascites is determined almost entirely by the serum protein concentration and portal pressure.[29]

Pitfalls in ascitic fluid total protein[3]

1. A patient with cirrhosis and a relatively high serum protein concentration will have a relatively high ascitic fluid protein

concentration. Almost 20% of samples in patients with cirrhosis will have relatively high ascitic fluid protein concentration > 2.5 g/dl.

2. The ascitic fluid total protein concentration does not increase during spontaneous bacterial peritonitis. It remains stable before, during of after infection. Infact patients with the lowest ascitic fluid protein concentrations are the most susceptible to spontaneous bacterial peritonitis.

3. During a 10 kg diuresis, the ascitic fluid total protein concentration doubles and 67% of such patients with cirrhotic ascites have a protein concentration greater than 2.5 g/dl by the end of diuresis.

4. In almost one third of patients with malignant ascites, the ascites is caused by massive liver metastasis or hepatocellular carcinoma and the ascitic fluid in these patients has a low protein concentration.

5. In cardiac ascites, the ascitic fluid protein concentration is greater than 2.5 g/dl.[27]

Therefore the exudate / transudate method of classification of ascites places many patients with cirrhosis and ascites and all patients with cardiac ascites in the exudates category and many patients with

malignant ascites and essentially all patients with spontaneously infected ascites in the transudate category. Clearly this method of classification is not useful.

Serum ascites albumin Gradient[3],[26],[30],[31],[38]

In contrast to the ascitic fluid total protein, SAAG classifies fluid by the presence or absence of portal hypertension and is much more physiologic. The Starling hypothesis is the underlying physiology behind the estimation of SAAG. The SAAG is based on oncotic – hydrostatic balance. Portal hypertension results in an abnormally high hydrostatic pressure gradient between the portal bed and the ascitic fluid. A similarly large difference must exist between the ascitic fluid and the intravascular oncotic forces. Albumin exerts greater oncotic pressure than that exerted by other proteins. Therefore the difference between the serum and the ascitic fluid albumin concentrations correlates directly with portal pressure.

The albumin gradient classifies cardiac ascites in the high SAAG category similar to cirrhotic ascites. The high SAAG of cardiac ascites is presumably the result of high right sided cardiac pressures.

Limitations of SAAG [19]:

1. The gradient may be falsely low, if the patients have a serum albumin < 1.1 g/dl and also in disease states with hyperglobulinemia.
2. Errors may occur if the albumin assay is inaccurate in the low range, when the samples are not withdrawn at relatively same time and if the patient is in shock.
3. A falsely high value of SAAG may occur in chylous ascites as lipid fractions tend to interfere with laboratory determination of albumin.

The following chart depicts the classification of ascites on the basis of the values of SAAG with a cut off value as 1.1 into high SAAG and low SAAG ascites.

Classification of Ascites by SAAG[3]

High gradient > 1.1 g / dl	**Low gradient < 1.1 g / dl**
Cirrhosis	Peritoneal Carcinomatosis
Alcoholic hepatitis	Tuberculous peritonitis
Cardiac ascites	Pancreatic ascites
Mixed ascites	Bowel obstruction or infarction
Massive liver metastasis	Biliary ascites
Fulminant hepatic failure	Nephrotic syndrome
Budd Chiari syndrome	Post operative lymphatic leak
Portal vein thrombosis	Serositis in connective tissue disorders
Sinusoidal obstruction syndrome	
Myxedema	
Fatty liver of Pregnancy	

Differentiation of Ascites using Ascitic fluid Tests: [17] ,[25]

Causes	**SAAG**	**AFTP**	**Other abnormalities**
Cirrhotic ascites	> 1.1	< 2.5	AFTP > 2.5 during diuresis
Cardiac ascites	> 1.1	> 2.5	
Peritoneal carcinomatosis	< 1.1	> 2.5	Malignant cells in ascitic fluid
Tuberculous peritonitis	< 1.1	> 2.5	WBCs >500 / cu.mm. Lymphocytic predominance
Chylous ascites	< 1.1	< 2.5	Milky ascitic fluid. Triglycerides > 200 mg / dl
Nephrotic syndrome	< 1.1	< 2.5	Proteinuria
Pancreatic ascites	< 1.1	> 2.5	Ascitic Fluid amylase (> 1000 U/L) > Serum amylase

Classification of Ascites based on SAAG and AFTP (11)

SAAG	**AFTP < 2.5 g / dl**	**AFTP > 2.5 g / dl**
>/= 1.1	Cirrhosis, Fulminant hepatic failure, Alcoholic hepatitis, Liver metastasis, Chronic Budd Chiari syndrome, Sinusoidal obstruction syndrome,Portal vein thrombosis.	Congestive heart failure, Myxedema, Acute Budd Chiari syndrome.
< 1.1	Nephrotic syndrome	Peritoneal Carcinomatosis, Tuberculous peritonitis, Pancreatic ascites, Chylous ascites.

Portal Hypertension:

Definition: (1)

Portal hypertension is defined as the elevation of the hepatic venous pressure gradient (HVPG) to > 5 mm Hg. Hepatic venous pressure gradient is equal to wedged hepatic venous pressure minus free hepatic venous pressure.

Hemodynamic considerations:

Pathophysiology of Portal hypertension: (7)

The pressure within the portal system is determined by the interaction of flow and vascular resistance. As these parameters change , so does the portal pressure. This relationship is expressed by Ohm's law.

D_0 = Q X R, where D_0 is change in pressure, Q is flow and R is resistance in a vessel.

Resistance is determined by several factors as expressed in Poiseuille's law,

R = 8 n 3.14 Ll r^4 , where n is the coefficient of viscosity, L is the vessel length and r , the vessel radius.

Within the liver, the viscosity and length of vessel are relatively constant, and changes in vascular resistance are mainly due to changes in radius.

The normal liver has a very low intrahepatic resistance. This inherent property of an extremely compliant hepatic circulation can maintain normal portal pressure within a wide range of portal flow. This capacity is lost in liver disease with dramatic increase in intrahepatic resistances. Along with the structural disturbances in cirrhosis, inflammatory changes in the hepatic venous tree and deposition of fibrous tissue around the terminal hepatic venules and adjacent sinusoids have been described.

In cirrhotic livers, intrahepatic resistance may also be affected by proliferation of myofibroblasts around the sinusoids and terminal hepatic venules resulting in increased contractility which may raise resistance and contribute to portal hypertension. These myofibroblasts are known as stellate cells. These are star shaped with branching arms and acquire contractile properties behaving in a similar manner to vascular pericytes.

Thus in response to vasoactive substances such as endothelin, these cells by their action on the sinusoids, at the microcirculatory

level, can increase resistance to portal blood flow. Sinusoids may be compressed by hepatocyte enlargement in regenerating parts of the liver. This can occur as a result of several toxic, infectious or metabolic insults to the parenchyma and may explain the portal hypertension in noncirrhotic conditions.

Theories of Portal hypertension:

Two major hypotheses have been advanced to explain this phenomenon.

Backward theory:

The backward theory postulates that portal hypertension is due to increased hepatic vascular resistance which develops as a specific response, so that in the presence of normal flow pressure increases. The hypertrophy of the myofibroblasts within the sinusoidal bed is one mechanism by which this could be achieved. In reality however, the portal and splanchnic circulation is not only markedly increased but hyperdynamic too, thus negating the likelihood that this theory can explain portal hypertension.

Forward theory:

The forward theory was initially postulated by Bantl et al. in 1883. He suggested that splenomegaly, portal hypertension and

cirrhosis were the result of increased splanchnic arterial blood flow. The theory suggests that the increased and hyperdynamic flow together with the decreased splanchnic precapillary resistance maintain portal hypertension in the face of extensive portosystemic shunting.

Recent concept:

More recently, Groszmann et al. and other workers have increasingly implicated that both the theories are being involved in the pathophysiology of the condition. It is currently believed that the principal and the initial abnormality is increased vascular resistance to portal flow and then portal hypertension is maintained by increased blood flow into the portal circulation, a phenomenon which has been confirmed conclusively both experimentally and clinically.

Causes of Portal Hypertension:

The causes are usually subcategorized as prehepatic, intrahepatic and posthepatic.

Prehepatic causes of portal hypertension are those affecting the portal venous system, before it enters the liver.

PREHEPATIC CAUSES
1. Portal vein thrombosis
2. Splenic vein thrombosis
3. Massive splenomegaly

Post hepatic causes encompass those affecting the hepatic veins and the venous drainage to the heart.

POST HEPATIC CAUSES
1. Budd chiari syndrome
2. Inferior venacaval webs
3. Cardiac causes- a. Restrictive cardiomyopathy b. Constrictive pericarditis c. Severe CCF

Intrahepatic causes account for over 95% of causes of portal hypertension and are represented by the major forms of cirrhosis. Intrahepatic cause of portal hypertension can be further subdivided into pre sinusoidal, sinusoidal and post sinusoidal causes.

HEPATIC CAUSES
I.Presinusoidal
a. Schistosomiasis
b. Congenital hepatic fibrosis
c. Sarcoidosis
d. Vinyl chloride
e. Drugs
II. Sinusoidal
a. Cirrhosis
b. Alcoholic hepatitis
c. Cystic liver disease
d. Partial nodular transformation of the liver
e. Metastatic malignant disease
III. Post sinusoidal
a. Hepatic sinusoidal obstruction
b. Veno occlusive syndrome

MATERIALS AND METHODS

The study of **'Serum Ascites Albumin Gradient in the etiological diagnosis of Ascites'** was carried out in the Department of General Medicine, Tirunelveli Medical College Hospital, Tirunelveli.

Setting : Medical Wards

Study Design : Single centre observational prospective hospital based study

Period of study : June 2008 to June 2009

Ethical approval : Obtained

METHODOLOGY

A total of fifty adult patients with ascites, admitted to the Department of General Medicine, Tirunelveli Medical College Hospital, Tirunelveli with in an one year period, whose etiological diagnosis had not been known previously were studied prospectively. The protocol was approved by the hospital's ethical committee and an informed consent was obtained from all patients.

On entry, a detailed history and clinical examination were conducted. The fifty patients who satisfied the set criteria were included in the study. Paired ascitic fluid and serum samples were collected from them simultaneously and were examined for ascitic fluid albumin, ascitic fluid total protein and serum albumin with established methods of estimation – Bromocresol green and Biuret methods as described by Varley et al.

Inclusion criteria:-

All patients with ascites due to any cause with normal coagulation profile.

Exclusion criteria:-

Ascitic patients with severe coagulopathy or disseminated intravascular coagulation (DIC).

Abdominal Paracentesis[3],[40]

After obtaining informed consent from the patient and relatives, diagnostic abdominal paracentesis was done. The patients were asked to empty the bladder, prior to the procedure.

The skin of the abdominal wall was disinfected with an iodine solution. The skin and subcutaneous tissue were infiltrated with a local anaesthetic. A special technique was followed to prevent the leakage of fluid after the needle was withdrawn. This technique of needle insertion (Z tract) was accomplished by displacing the skin approximately 2 cms downward and then slowly inserting the paracentesis needle mounted on the syringe held in the other hand. The paracentesis needle is a steel 22 gauge needle about 1.5 inch in length. The hand holding the syringes was used to stabilize the syringes and to retract the plunger simultaneously. The skin was released only after the needle had penetrated the peritoneum. When the needle was ultimately removed, the skin resumed the original position and sealed the needle pathway.

The needle was advanced slowly through the abdominal wall. Slow insertion helped to allow the bowel to move away from the needle thereby avoiding bowel puncture.

Site of needle insertion:-

The needle was inserted into the left lower quadrant rather than the right lower quadrant because the caecum may be distended with gas from lactulose therapy. In the presence of a surgical scar, the needle was placed several centimeters from the scar.

The ascitic fluid collected was sent for cell count in an EDTA bottle, biochemical analysis including total protein and albumin in a plain bottle and for cuture in a blood culture bottle.

Simultaneously blood samples were collected from the patients and were sent for the estimation of serum albumin to the laboratory.

Calculation of SAAG

The serum ascites albumin gradient was calculated after measuring the serum and ascitic fluid albumin concentrations and simply subtracting the ascitic fluid value from the serum value.

To increase the accuracy of SAAG, specimens of serum and ascitic fluid were obtained simultaneously.

Correction of SAAG

To correct the SAAG in the setting of a high serum globulin level the following formula was used.

Corrected SAAG = Uncorrected SAAG x 0.16 x (Serum globulin + 2.5)

Serum hyperglobulinemia (Serum globulin> 5 g/dl) leads to a high ascitic fluid globulin concentration and can narrow the albumin gradient by contributing to the oncotic forces. A narrow gradient caused by high globulin levels occurs in one percent of ascitic fluid specimens.

Albumin estimation :- BCG method

The serum and ascitic samples for albumin are fed into the autoanalyser.

Principle

Albumin in a buffered solution reacts with the anionic bromocresol green (BCG) with a dye binding reaction to give a proportionate green colour which is measured at 628 nm (600-650nm)

Reagents.

Reagent 1 (Bromocresol Green):

Succinic acid 94 mmol/L

Sodium hydroxide 10.2 mmol/L

BCG 0.149 mmol/L

Standard (Albumin 5g/dl)

BSA 50g/L

Total protein (Biuret method)

Principle:

Peptide bonds of protein form a blue violet coloured complex with cupric ions in an alkaline medium. The intensity of the colour is proportional to the number of peptide bonds and the colour is read at 540 nm.

Reagents.

Reagents 1 (Biuret reagent)

Sodium hydroxide 3.8 mol/L

Potassium Sodium tartrate 0.1 mol/L

Cupric sulfate 33 mmol/L

Potassium iodide 30 mmol/L

Reagent 1 A (Surfactant)

Surfactant 20 g/l

Standard (total protein 6g/dl)

BSA 60 g/l

All the 50 patients further underwent ultrasonogram abdomen which revealed the ultimate diagnosis for confirmation and comparing the diagnostic accuracies of SAAG and ascitic fluid protein.

Ultrasonography of the liver and portal venous system, which is a noninvasive imaging modality, helped to establish the diagnosis of portal hypertension. USG diagnosis of portal hypertension was based on demonstration of

a. Dilated collaterals around the gastroesophageal junction and splenic hilum,

b. Splenomegaly and dilated portal vein >14 mm in diameter and splenic vein >12 mm.

It also helped in establishing the etiology of portal hypertension by giving information about

a.Hepatic architecture (altered echopattern with nodularity indicates cirrhosis, normal echopattern in extrahepatic portal vein obstruction and non cirrhotic portal fibrosis) ,

b. Patency of the portal and splenic veins (portal vein thrombosis and portal cavernoma diagnostic of EHPVO) and

c. Patency of hepatic veins and IVC. (thrombosis or Budd chiari syndrome)

OBSERVATION AND RESULTS

The results of the diagnostic ascitic fluid aspiration and the ascitic fluid analysis in all the fifty selected patients are being interpreted here.

The ascitic fluid specimens of fourty eight patients were straw coloured, whereas two specimens were hemorrhagic. After complete workup, one turned out to be a case of chronic calcific pancreatitis and and the other was a case of peritoneal carcinomatosis with primary in the large intestine.

Table:1 Sex Distribution

Males	26
Females	24

Table: 1 describes the distribution of ascites among the males and the females in the selected study group. The distribution of ascites among the males and the females was more or less equal with 26 males and 24 females with a sex ratio of 1.08.

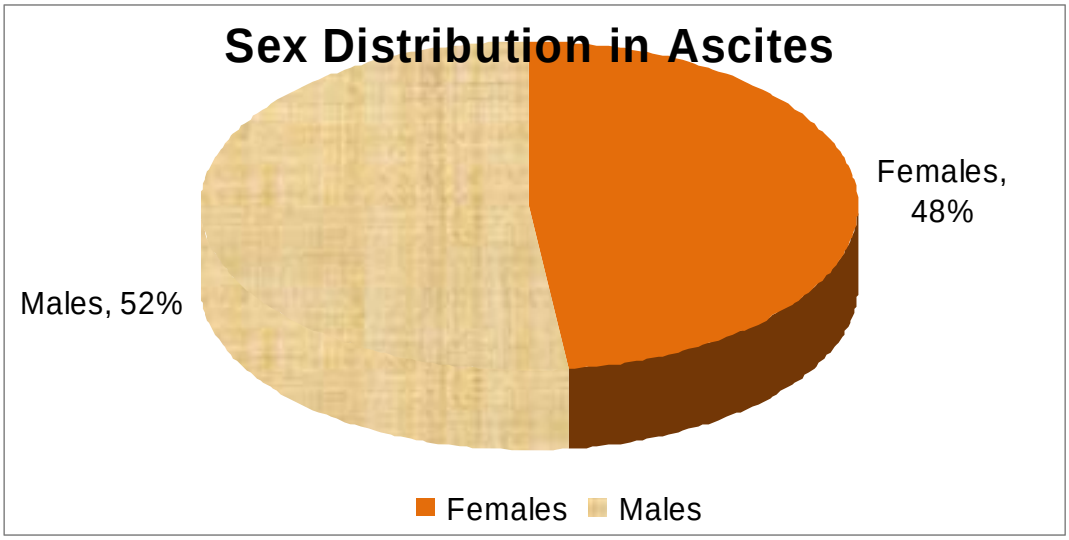


Table:2 Age wise distribution

Age(years)	Total
11- 20	2
21- 30	3
31- 40	10
41- 50	9
51- 60	8
61- 70	14
71- 80	4

Table: 2 outlines the distribution of ascites among the different age groups. It is quite interesting to note that the incidence of ascites increases as the age advances and the total number of cases peaks around 60 -70. The majority of the cases i.e. 45/50 (90%) are aged above 30 years, with a minority i.e. 5/50 (10%) below 30 years of age.

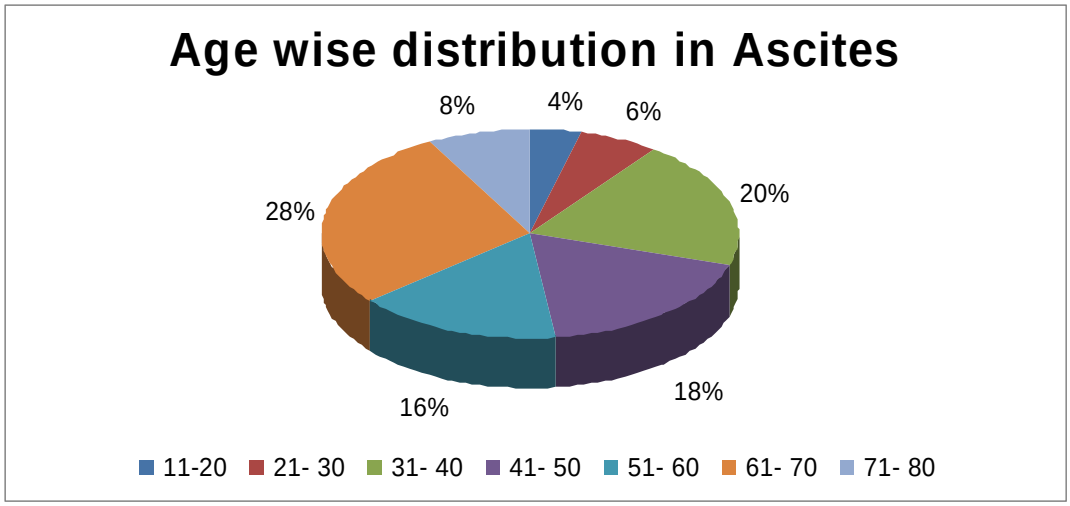


Table:3 Comparison of age wise and sex wise distribution

Age (years)	Total	Female	Male
11- 20	2	2	0
21- 30	3	3	0
31- 40	10	6	4
41- 50	9	3	6
51- 60	8	4	4
61- 70	14	6	8
71- 80	4	0	4

Table:3 gives an outlook of the distribution of the age wise distribution of ascites among males and females. The minor group (10%) who presented below the age of thirty years were all females with no males. As the age advanced beyond 30 years of age, the incidence increased in both males and females with a maximum of males compared to females. Thus the incidence of ascites was more

among females in the younger age, whereas the incidence though increased both in males and females as the age advanced, it was higher in males (i.e.26/50 = 52%) when compared to females (i.e. 19/50 = 38%).

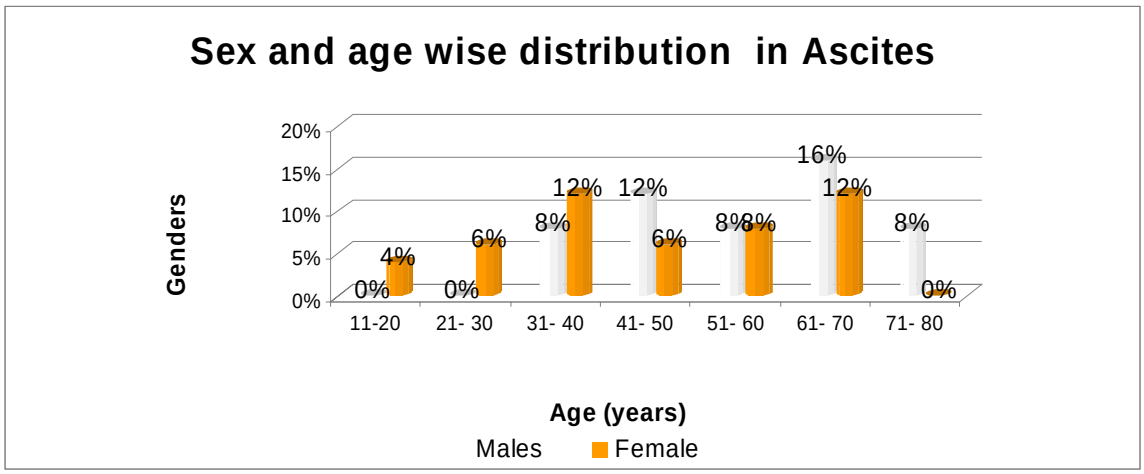
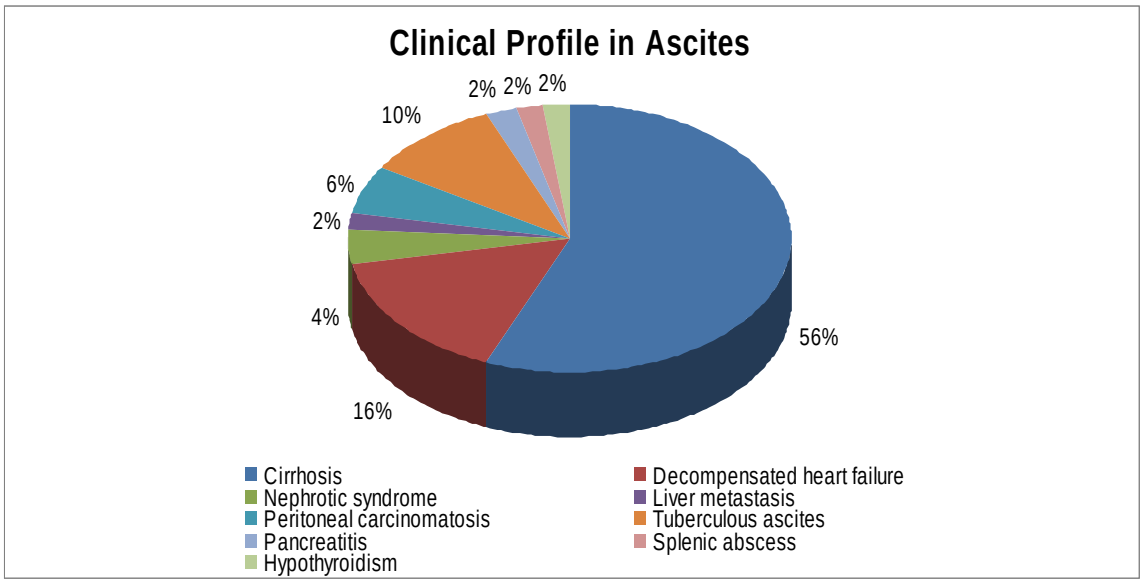


Table: 4 Clinical profile:

Etiology	Total number
Cirrhosis	28
Decompensated heart failure	8
Nephrotic syndrome	2
Liver metastasis	1
Peritoneal carcinomatosis	3
Tuberculous ascites	5
Pancreatitis	1
Splenic abscess	1
Hypothyroidism	1

Table: 4 interprets the etiological distribution of ascites among the study group. Considering the etiology of ascites in the population studied, cirrhosis of the liver (28 cases) ranked first followed by decompensated heart failure (8 cases), tuberculous peritonitis (5 cases) and malignant ascites (4 cases). The other causes were nephrotic syndrome (2 cases), splenic abscess (1 case), pancreatitis (1 case), spontaneous bacterial peritonitis (1 case) and hypothyroidism (1 case).



The cases who presented with ascites due to decompensated heart failure were evaluated. Among the 8 cases, there were 2 cases of valvular heart disease, 2 cases of corpulmonale, 2 cases of coronary artery disease with ischemic cardiomyopathy, 1 case of dilated cardiomyopathy and another case of restrictive cardiomyopathy.

There were 4 cases of malignant ascites among which 3 were cases of peritoneal carcinomatosis and the other one was a primary colonic carcinoma with secondaries in liver. The primary tumours of peritoneal carcinomatosis were in ovary, stomach and large intestine.

Table:5 Comparison of sex distribution and etiology of ascites

Etiology	**Males**	**Females**	**Total**
Cirrhosis	19	9	28
CCF	2	6	8
Nephrotic syndrome	1	1	2
Liver metastasis	0	1	1
Peritoneal carcinomatosis	1	2	3
TB Peritonitis	1	4	5
Splenic abscess	1	0	1
Pancreatitis	0	1	1
Hypothyroidism	0	1	1

Table: 5 gives an outline of the etiological distribution of ascites among both males and females. The most common cause of ascites among both the males and females was cirrhosis. Though cirrhosis was the common cause in both the genders, it constituted the major cause in males (i.e. 19/26=73%). However in females, the noncirrhotic

cases taken altogether, constituted the major group (i.e. 15/24=67%), whereas the cirrhotics constituted only the reminder (i.e. 9/24=33%).

Among the non cirrhotic causes, decompensated heart failure topped the list with females about 75% (6/8) compared to males, followed by tuberculous peritonitis with females amounting 80% (4/5) and malignant ascites with 50% females (2/4).

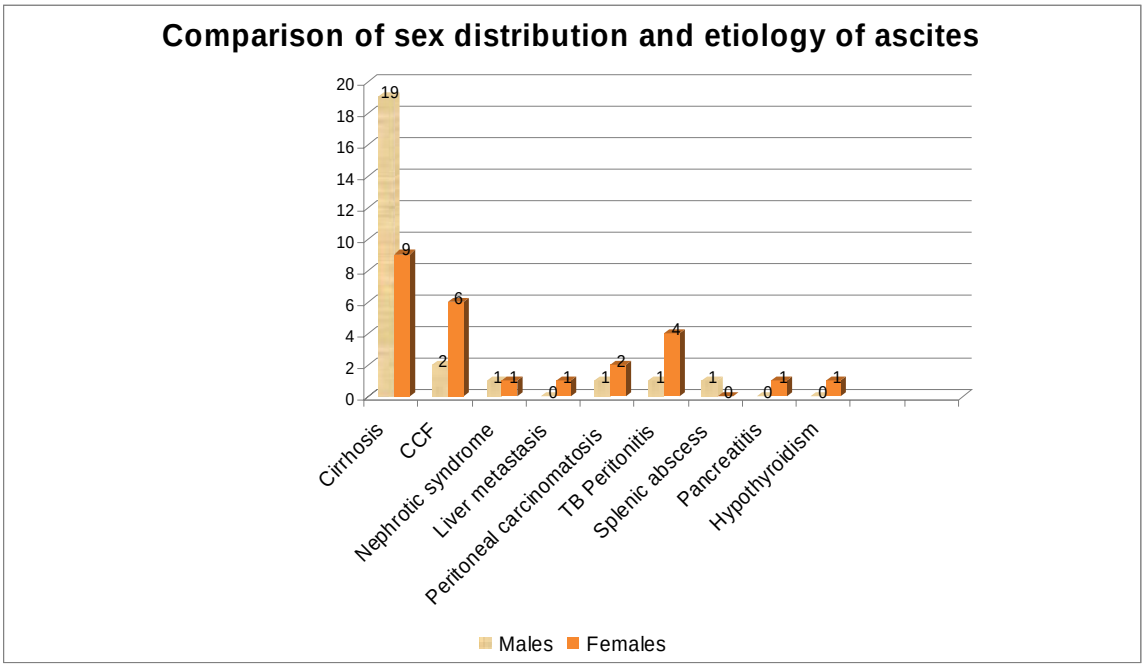


Table:6 Comparison of etiology of ascites and age wise distribution in males

Etiology	11-20	21-30	31-40	41-50	51-60	61-70	71-80	Total
Cirrhosis	0	0	3	6	3	6	1	19
CCF	0	0	0	1	0	1	0	2
Nephrotic syndrome	0	0	1	0	0	0	0	1
Liver metastasis	0	0	1	0	0	0	0	1
Peritoneal Ca	0	0	0	0	0	0	1	1
TB Peritonitis	0	0	0	0	1	0	0	1
Splenic abscess	0	0	0	0	0	0	1	1

Table:6 explains the distribution of ascites among different age groups in males. In males, cirrhosis is the leading cause peaking in the age group (61-70) followed by the age group (41-50). All the other causes of ascites like decompensated heart failure, hepatocellular carcinoma, peritoneal carcinomatosis, tuberculous peritonitis and splenic abscess presented beyond 40 years of age. Something interesting here is that no men presented below 20 years of age.

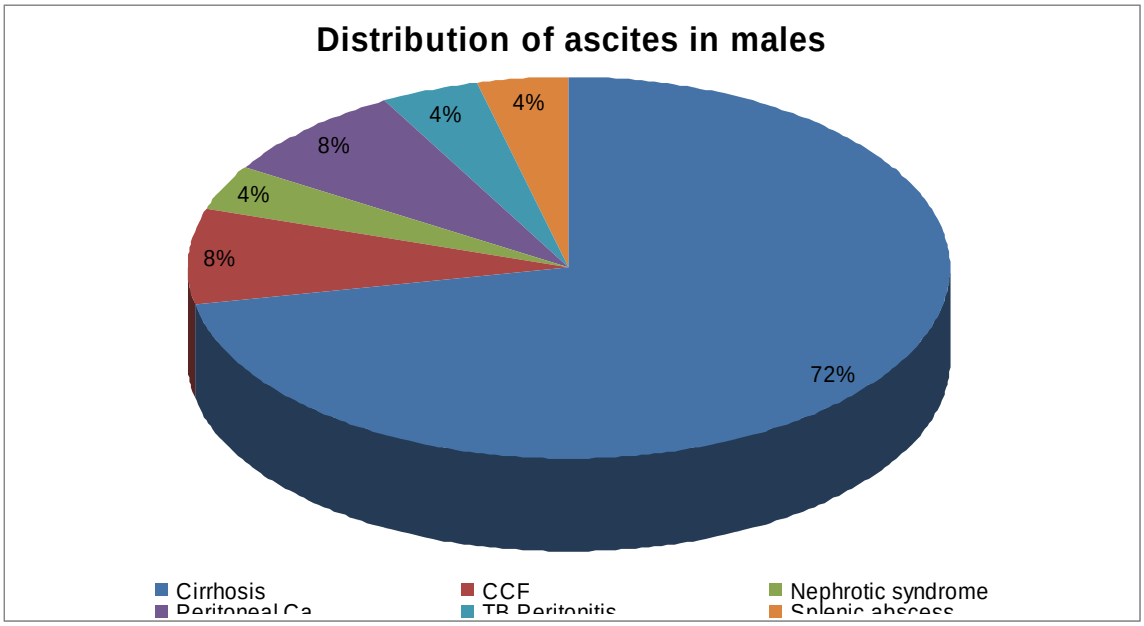


Table:7 Comparison of etiology of ascites and age wise distribution in females

Etiology	11-20	21-30	31-40	41-50	51-60	61-70	71-80	Total
Cirrhosis	0	0	3	0	2	4	0	9
CCF	0	1	1	1	1	2	0	6
Nephrotic syndrome	0	0	1	0	0	0	0	1
Peritoneal Ca	0	0	0	1	0	0	1	2
TB Peritonitis	2	1	0	0	1	0	0	4
Pancreatitis	0	1	0	0	0	0	0	1
Hypothyroidism	0	0	0	0	0	1	0	1

Table:7 explains the distribution of ascites among different age groups in females. About 42% women (10/24) presented below 40 years of age and the remaining 58% women presented above 40 years of age. Tuberculous peritonitis was common amongst the younger individuals when compared to the old, whereas cirrhosis was common among the older individuals. Decompensated heart failure was equally prevalent in all age groups. Congestive cardiac failure and tuberculous peritonitis were common amongst females (10/24=42%) compared to males (3/26=12%).

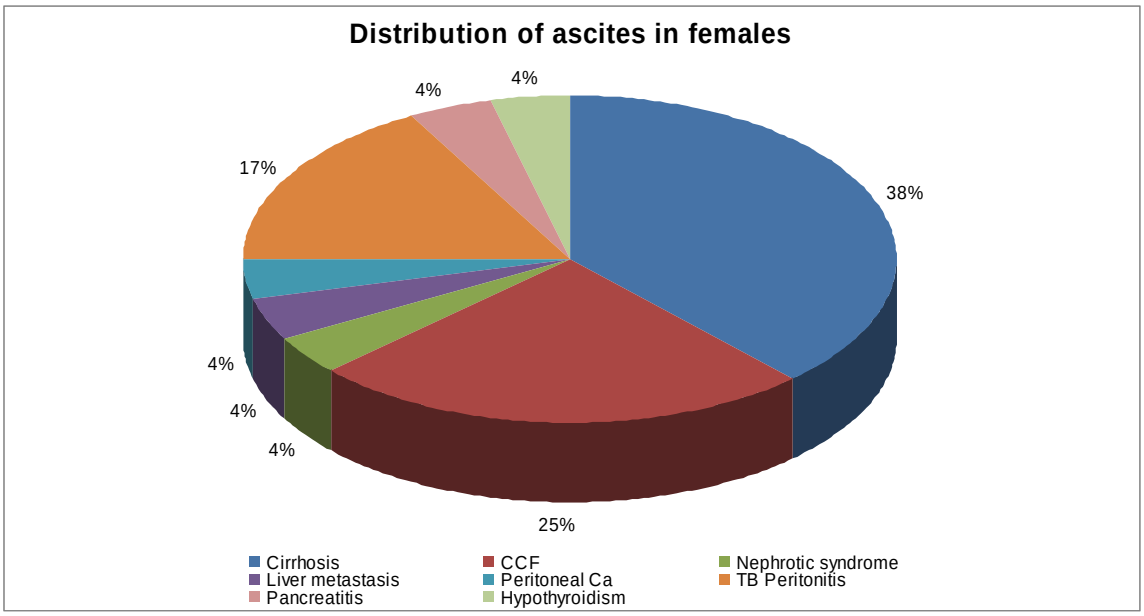


Table: 8 Distribution of ascites on the basis of SAAG

Etiology	SAAG>/=1.1	SAAG<1.1
Cirrhosis	26	2
CCF	8	0
Nephrotic syndrome	0	2
Liver metastastasis	1	0
Peritoneal carcinomatosis	0	3
TB ascites	1	4
Pancreatitis	0	1
Splenic abscess	0	1
Hypothyroidism	1	0

Table:8 groups the individuals with ascites in the study population into high SAAG group and low SAAG group with a cut off value of 1.1.About 74% of the people were in high SAAG group and the left out 26% were in low SAAG group.

Cirrhotic patients (26 cases), 8 cases of decompensated heart failure, a case each of liver metastasis, TB ascites and hypothyroidism had high SAAG ascites.

4 cases of TB ascites, 3 cases of peritoneal carcinomatosis, 2 cases of nephrotic syndrome, 2 cases of cirrhosis, 1 case each of pancreatitis and splenic abscess had low SAAG ascites.

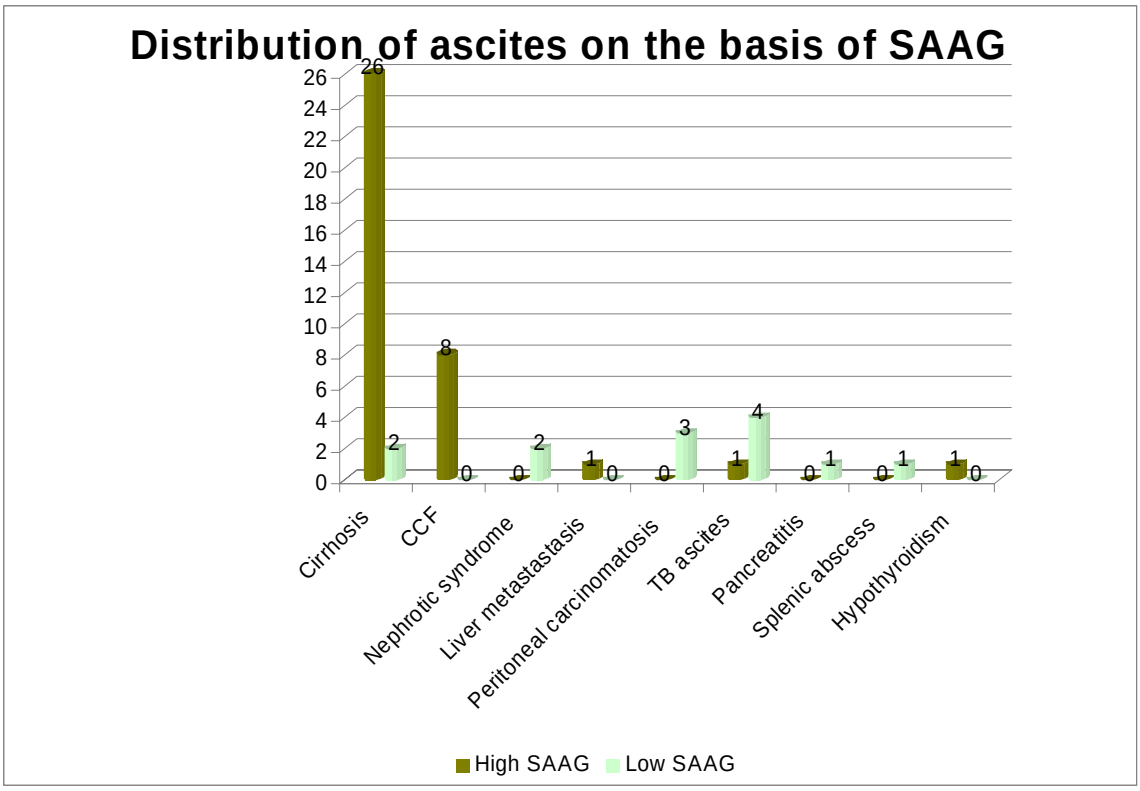


Table: 9 Distribution of ascites on the basis of ascitic fluid total protein

Etiology	AFTP>/=2.5	AFTP<2.5
Cirrhosis	9	19
CCF	4	4
Nephrotic syndrome	1	1
Liver metastasis	0	1
Peritoneal carcinomatosis	3	0
TB peritonitis	4	1
Pancreatitis	1	0
Splenic abscess	1	0
Hypothyroid	1	0

Table:9 classifies the ascites of the patients into two groups as exudative and transudative with the cut off of ascitic fluid total protein as >/=2.5 and <2.5 respectively. 48% of cases presented as exudative and 52% of cases had transudative ascites.

After evaluating the patient with imaging studies and coming to the conclusion of the etiology, the patients were further classified into high SAAG or low SAAG, depending on the pathophysiology of ascites, whether related or unrelated to portal hypertension and exudative ascites or transudative ascites which are depicted in tables 10 & 11.

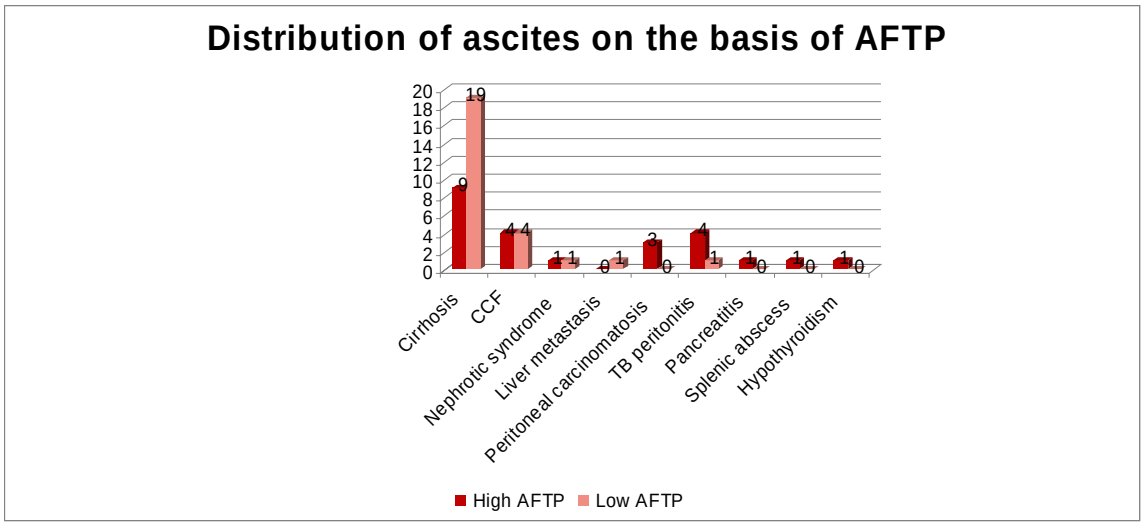


Table:10 Classification of ascites depending on the Pathophysiology

High SAAG	No.	Low SAAG	No.
Cirrhosis	28	**Splenic abscess**	1
CCF	8	**Pancreatitis**	1
Liver metastasis	1	**Peritoneal carcinomatosis**	3
Hypothyroidism	1	**TB peritonitis**	5
		Nephrotic syndrome	2

Table 10: groups the ascites into high SAAG and low SAAG depending on the pathophysiology. Cirrhosis, decompensated heart failure, liver metastasis and hypothyroidism were grouped under high SAAG ascites. Peritoneal carcinomatosis, tuberculous ascites, nephrotic syndrome, splenic abscess and pancreatitis were grouped under low SAAG ascites.

Table: 11 Classification of ascites as exudative or transudative

Exudate	No.	Transudate	No.
Peritoneal carcinomatosis	3	**Cirrhosis**	28
Liver metastasis	1	**Nephrotic syndrome**	2
TB Peritonitis	5	**CCF**	8
Splenic abscess	1		
Pancreatitis	1		
Hypothyroidism	1		

Table 11 groups the ascites as transudative and exudative after the etiology being identified. Cirrhosis, decompensated heart failure and nephrotic syndrome were grouped under transudative ascites whereas malignant ascites, tuberculous ascites, splenic abscess, hypothyroidism and pancreatitis were grouped under exudative ascites.

Table: 12 Comparison of SAAG and Portal hypertension

Pathophysiology	**High SAAG**	**Low SAAG**
Portal HT	36 (True positive)	2 (False negative)
Non Portal HT	1 (False positive)	11 (True negative)

On comparing the high SAAG values and the presence of portal hypertension, 36 patients with high SAAG had a pathophysiology related to portal hypertension i.e true positive (a), whereas only one patient with high SAAG did not have portal hypertension i.e false positive (b). On the other hand, 11 patients with low SAAG did not have portal hypertension i.e true negative (d) and 2 patients with low SAAG had portal hypertension as its pathophysiology i.e false negative (c).These results are depicted in the **Table:12**.

Table:13 Comparison of AFTP and exudative/transudative

	AFTP >2.5	**AFTP<2.5**
Exudate	10 (true positive)	2 (false negative)
Transudate	14 (false positive)	24 (true negative)

Comparing the values of ascitic fluid total protein and exudative/ transudative ascites , 12 patients with AFTP > 2.5 had exudative ascites i.e true positive (a), whereas 16 patients with AFTP> 2.5 had transudative ascites i.e false positive (b). However 20 patients with AFTP <2.5 had transudative ascites i.e true negative (d) and 2 patients with AFTP < 2.5 had exudative ascites i.e false negative (c). These results are depicted in **Table:13.**

1.Sensitivity is calculated by dividing true positive by the sum of true positive and false negative. i.e. (a / a+c)x 100. (14)

2.Specificity is calculated by dividing true negative by the sum of true negative and false positive. i.e. (d/ d+b)x 100.

3.Positive predictive value is calculated by dividing true positive by the sum of true positive and false positive i.e. (a/ a+b) x 100

4.Negative predictive value is calculated by dividing true negative by the sum of true negative and false negative i.e. (d/d+c) x 100

5.Diagnostic accuracy is calculating by dividing the sum of true positive and true negative by the total number of cases and multiplying by 100.

All the parameters were calculated separately for SAAG and ascitic fluid total protein using the above formulae.

ASCITIC FLUID TOTAL PROTEIN (AFTP)

Sensitivity of AFTP = 10/(10+2) x 100 = 83 %

Specificity of AFTP = 24/(24+14) x 100 = 63%

Positive predictive value of AFTP = 10/(10+14) x 100 = 42%

Negative predictive value of AFTP = 24/(24+2) x 100 = 92%

SERUM ASCITES ALBUMIN GRADIENT (SAAG)

Sensitivity of SAAG= 36/(36+2) x 100 =94%

Specificity of SAAG= 11/(11+1) x 100 = 91%

Positive predictive value of SAAG = 36/(36+1) x 100 = 97%

Negative predictive value of SAAG = 11/(11+2) x 100 = 85%

DIAGNOSTIC ACCURACY

Diagnostic accuracy =(True positive + True negative)/Total number of cases

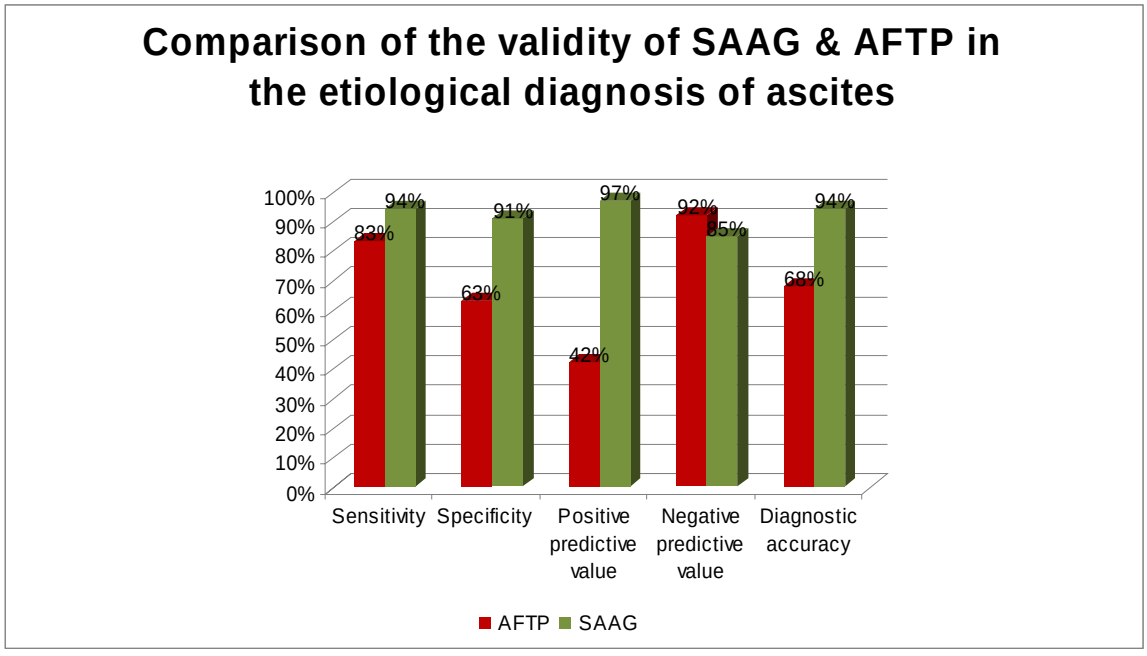
Diagnostic accuracy of AFTP = (10+24)/50 x 100 = 68%

Diagnostic accuracy of SAAG = (36+11)/50 x 100 = 94%

Table: 14 Comparison of AFTP & SAAG

Parameters	AFTP	SAAG
Sensitivity	83%	94%
Specificity	63%	91%
Positive predictive value	42%	97%
Negative predictive value	92%	85%
Diagnostic accuracy	68%	94%

SAAG IS BETTER THAN AFTP



The five variables calculated for both AFTP and SAAG are depicted in **table: 14.** At a glance from this table, one could understand easily and with no doubt that SAAG is better than AFTP in determining the etiology of ascites, which is the aim of the present study.

DISCUSSION

The results of the study "SAAG in the etiological diagnosis of ascites" conducted in the medical wards of Tirunelveli medical hospital has yielded an etiological profile of the entire study group as follows :

1.Liver cirrhosis – 56%

2.Decompensated heart failure – 16%

3.Tuberculous peritonitis – 10%

4.Malignant ascites – 8% including 3 cases of peritoneal carcinomatosis and 1 case of malignant deposit in liver

5. Nephrotic syndrome – 4%

6. Splenic abscess – 2%

7. Pancreatitis – 2%

8. Hypothyroidism – 2%

In a study[52] conducted by U.H.Malabu et.al.,I.O.Olubuyide et.ai., M.E.Shaibu et.al and F. Olawuyi et.al. (2006) in the gastroenterology unit, department of medicine, University college Hospital, Ibadan, Nigeria, the clinical profile was as follows : 44% liver cirrhosis, 23% TB peritonitis, 22% Malignant ascites , 6% heart diseases and 5% nephrotic syndromes.

In another group of 132 people studied[53] by Al-Knavy BA et.al. at the division of Gastroenterology, King Saud University, Abha, Saudi Arabia, the clinical ranking and profile were similar to the previous one with 69.7% liver cirrhosis, 10.6% peritoneal tuberculosis, 9.1% malignant ascites, 7.6% decompensated cardiac failure and 3% nephrotic syndrome.

In contrast to the two studies discussed above, decompensated heart failure ranked the second instead of tuberculous peritonitis, in the present study group. On the other hand the major causes of ascites are liver cirrhosis amd malignant ascites in the western population, whereas tuberculous peritonitis leads the list in the Asians and Blacks.

However it is important to note that there is a limitation to such studies in general. Statistics derived from hospital figures are biased and are only an approximate guide to the incidence of the disease in a community. What is seen in hospitals may represent only the tip of an iceberg. The present data must be interpreted in the knowledge of the defects inherent to such studies.

The clinical profile of the low SAAG ascites in the present study group was 38% of tuberculous peritonitis, 25% of peritoneal carcinomatosis, 15% of nephrotic syndrome and other causes like pancreatitis and splenic abscess which accounted for 7% each. The present study is comparable to a study[50] conducted by Fariborz Mansour – Ghanaei et al., Afshin Shafaghi et al., Amir- Hossein Bagherzadeh et al., Mohammad- Sadegh Fallah et al. among 148 patients over a 7 years period at the Gastrointestinal and liver diseases research centre, Gullan University of medical sciences, Gullan Province, Iran, which concluded that Tuberculous peritonitis should be considered in all patients with low gradient ascites in the developing countries. This is in contrast to the study[36] conducted by Runyon et al. which stated malignant ascites as the commonest cause of low SAAG ascites in the developed countries.

Myxedema ascites is a rare entitiy and hypothyroidism as a cause of ascites accounts for less than one percent. A case report[54] and review literature by Jeong – Seon Ji et al. and colleagues at the department of internal medicine and Pathology, College of Medicine, The Catholic University of Korea, Seoul, Korea had stated that in a review of 51 well documented cases of myxedema ascites the mean SAAG and ascites were 1.5 & 3.9 g/dl respectively. Similarly the sixty eight years old hypothyroid female in our study, presented with high protein and high SAAG ascites.

In the present study, the patients with malignant ascites presented as two groups – one with high SAAG ascites comprising 1 case of secondaries liver comprising about 25%. The other group presented with low SAAG ascites consisting of 3 cases of peritoneal carcinomatosis comprising about 75%. A similar one[51],” the study of the clinical pattern of ascites due to malignancy” was conducted in Qatar, by Khan F Y et al.,Ahmed M S et al., Lotf A Q et al. and Acsamawi M et al. during the year 2005 -2006, at Hamad General Hospital among 22 patients. The study revealed that SAAG was able to discriminate peritoneal carcinomatosis from other types of malignant ascites, since it is related to the genesis of ascites and it is

very crucial in clinical practice. The diagnostic accuracy of SAAG in malignant ascites is 100% in our present study .

The results of the application of the two tests of interest, i.e

1. Serum ascites albumin gradient (SAAG) &
2. Ascitic fluid total protein (AFTP)

in the categorization of etiology of ascites in the study population are expressed in terms of sensitivity, specificity , positive predictive value, negative predictive value and diagnostic accuracy calculated by the appropriate formulae as already discussed.

The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of SAAG are 94%, 91%, 97%, 85% and 94% respectively as compared to 83%, 63%, 42%, 92% and 68% respectively with ascitic fluid total protein (Table:14).These results clearly demonstrate that SAAG offers an excellent discrimination of the causes of ascites. Similar observations have been reported by other studies too.

In the study [52] conducted by Al-Kanvy BA et.al. in Saudi Arabia, two other parameters i.e. ascitic fluid lactic dehydrogenase and ascitic to serum ratio of total protein , in addition to SAAG and AFTP were compared. Among all the four, SAAG had the highest

poitive and negative predictive values (80% & 98%) against that of ascitic fluid total protein (68% & 96%).

There are two Indian studies[51],[39] which were conducted in Aligarh and Allahabad regarding the comparison of the accuracies of SAAG and AFTP in diagnosing the etiology of ascites. In the study of 76 patients at the department of medicine, JN medical college, Aligarh Muslim University by M. Beg et al., S.Hussain et al., N.Ahmad et al. and N.Akhtar et al. the diagnostic accuracy and sensitivity of SAAG were 96% & 68% against the respective values 68% & 66% of AFTP. In the other study, conducted at the department of Gastroenterology and Pathology, M.L.N Medical college, Allahabad, by Gupta.R et al., Misra.SP et al., Dwivedi.M et al., Misra.V et al., Kumar.S et al. and Gupta SC et al., the diagnostic accuracies of AFTP and SAAG were found to be 88% & 92% respectively.

All these studies were based on the initial study[26] conducted by Bruce A. Runyon et al., Agnes A.Montano et al.,Evanengolos A. Akriviadis et al., Mainor R.Antillon et al.,Michelle A.Irving et al. and John G. McHutchison et al. among 901 patients in the University of

Iowa, Iowa city in the year 1992. The diagnostic accuracy of SAAG and ascitic fluid total protein were 96.7% and 55.6% respectively.

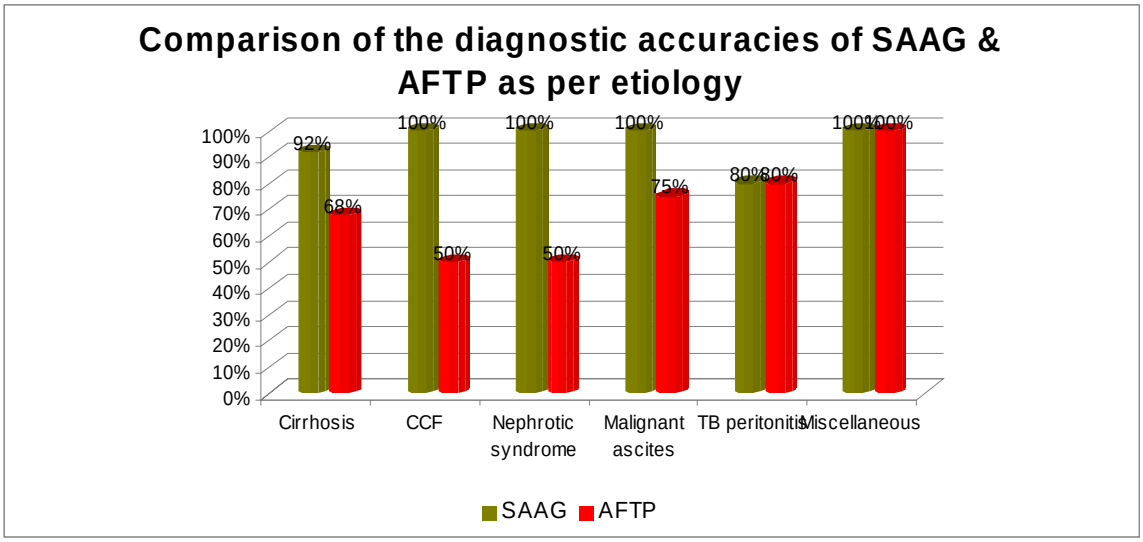
In another study[38] conducted among 51 patients by Akriviadis EA et al., Kapnas D. et al., Hadjigraviel M. et al., Missiou A. et al. and Goulis J et al. in the University of Thressaloniki, Hippocratical Hospital, Greece the diagnostic accuracy of SAAG was found to be 98%when compared to 52 – 80% in the four other diagnostic markers compared. (Ascitic fluid total protein, Ascites/Serum total protein ratio, Ascitic lactate dehydrogenase concentration and Ascites/Serum lactate dehydrogenase ratio).

Table:15 Comparison of the

diagnostic accuracies of SAAG & AFTP as per etiology

Etiology	**SAAG**	**AFTP**
Cirrhosis	92%	68%
CCF	100%	50%
CRF	100%	50%
Malignant ascites	100%	75%
TB peritonitis	80%	80%
Miscellaneous (Splenic abscess, Hypothyroidism & Pancreatitis)	100%	100%

$t = 2.72$ ($p < 0.05$)



The diagnostic accuracy of SAAG and AFTP were calculated separately (Table:15) for each cause in the present study and they were compared statistically using student's t test to determine the 95% confidence interval. A p value < 0.05 is considered significant.

The calculated t value is 2.72. ($p < 0.05$). For 10 degrees of freedom the table value is 2.23 at 5% level of significance, which is lesser than 2.72. So the data is significant at 5% level of significance and implies that SAAG is a better diagnostic measure than ascitc fluid total protein.

Thus Serum ascites albumin gradient (SAAG) is the single best test against ascitic fluid total protein (AFTP), in the differential diagnosis of ascites. The terms exudative and transudative can be replaced by high SAAG and low SAAG ascites. This result is similar to the results of all the studies conducted[42],[43],[48],[47],[45] .

CONCLUSION

The study "Serum ascites albumin gradient in the etiological diagnosis of ascites" conducted among the fifty inpatients with ascites, in the wards of the Department of General Medicine, at Tirunelveli Medical College Hospital has concluded that

1. The sensitivity and specificity of SAAG in the differentiation of different types of ascites are 94% and 91% respectively.

2. The accuracy of SAAG in the etiological diagnosis is 94%.

3. The serum ascites albumin gradient (SAAG) is superior to ascitic fluid total protein (AFTP) in the differential diagnosis of ascites and it is statistically significant.

FUTURE PERSPECTIVE

A number of studies since 1991 till date have proved the efficacy of SAAG in the differential diagnosis of ascites. As a result, SAAG has started replacing the age old exudate-transudate concept in the etiological diagnosis of ascites, in most of the institutions.

Hence, further studies[37],[49] are aimed at concentrating the correlation between the value of SAAG and the complications of portal hypertension like esophageal varices leading on to upper gastrointestinal bleeding.

In case, these studies could yield certain satisfactory and significant results, the SAAG value can be used as a screening tool to predict upper GI bleed. Moreover, the patients with portal hypertension could be put on prophylactic therapy considering the significant SAAG value, so that the mortality and morbidity in these patients can be reduced.

In a nutshell, further studies are expected to extend the use of SAAG, beyond the differential diagnosis of ascites, such as complications and management of ascites.

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PROFORMA

Name : **Age :** **Sex :**

Place : **Occupation:**

Chief complaints:

Past History:

Personal history:

General examination:

Examination of Major systems:

Abdominal examination:

Examination of the Cardiovascular system:

Examination of the Respiratory system:

Examination of the Central nervous system

Investigations:

1. Urine albumin, 24 hours urinary protein, sugar, deposits, bile salts and bile pigments.
2. Complete blood count
3. Blood urea, sugar, Serum creatinine and electrolytes.
4. Liver function tests – Serum bilirubin, SGOT, SGPT, alkaline phosphatase, Total protein, Albumin, Globulin, Prothrombin time.
5. Ascitic fluid analysis – cell count, cytology, protein, albumin, glucose, amylase, adenosine deaminase, Gram's stain, AFB & culture and sensitivity.
6. ECG in all leads
7. Xray chest PA view
8. USG Abdomen and Pelvis
9. CT scan abdomen and Echocardiogram in selected cases
10. Thyroid Profile
11. Serum amylase
12. Serum adenosine deaminase
13. Upper GI endoscopy
14. FNAC of the peritoneal nodules.

MASTER CHART

Sl. No	Name	IP no	Age	Sex	Serum albumin	Ascitic fluid albumin	SAAG	Ascitic fluid total protein	Etiology
1.	Muthiah	26176	32	M	2.5	0.5	1.0	2.0	Nephrotic syndrome
2.	Mohamed Yosuf	25199	55	M	3.7	1.2	2.5	3.7	Cirrhosis
3.	Ramakrishnan	35307	62	M	2.8	1.1	1.7	2.4	Cirrhosis
4.	Jenetus	29330	33	M	2.9	0.3	2.6	0.6	Cirrhosis
5.	Subramanian	22925	45	M	2.9	2.1	0.8	5.1	Cirrhosis
6.	Parvathiraja	28969	42	M	2.6	1.1	1.5	2.3	Cirrhosis
7.	Ganapathy	30412	36	F	1.6	0.5	1.1	2.8	Cirrhosis
8.	Shenbagammal	31210	62	F	3.7	2.4	1.3	4.0	RHD/AF/CCF
9.	Ganapathy	31215	32	F	2.0	1.0	1.0	3.0	Nephrotic syndrome
10.	Kavitha	31320	32	F	3.0	1.0	2.0	2.0	CCF Corpulmonale
11.	Lakshmi	31414	75	F	3.0	2.0	1.0	4.9	Peritoneal Carcinomatosis
12.	Subramanian	31435	68	M	2.5	1.1	1.4	2.0	DCM
13.	Velladurai	31472	69	M	3.0	0.7	2.3	2.0	Cirrhosis
14.	Arulraj	31489	42	M	2.1	0.3	1.8	0.4	Cirrhosis
15.	Velladurai	32459	42	M	3.0	1.8	1.2	3.4	COPD/ Corpulmonale
16.	Paldurai	33422	72	M	3.6	2.6	1.0	4.9	Peritoneal Carcinomatosis
17.	Gomathy	34868	51	F	2.3	0.6	1.7	1.0	Cirrhosis
18.	Lakshmi	34629	62	F	3.8	3.1	0.7	7.0	Cirrhosis
19.	Prema	34601	13	F	4.2	2.6	1.6	6.8	TB ascites
20.	Chinthanamma	34072	35	F	2.0	0.6	1.4	1.0	Cirrhosis
21.	Katheeja Beevi	32766	55	F	2.1	0.7	1.4	2.1	Cirrhosis
22.	Balu	33901	53	M	3.5	2.2	1.3	6.3	Cirrhosis

23.	Lakshmi	34977	65	F	3.0	1.8	1.2	2.0	Cirrhosis
24.	Thilagar	35109	72	M	3.2	2.4	0.8	4.0	Splenic abscess
25.	Ramajeyam	33424	72	M	3.2	0.5	2.7	2.3	Cirrhosis
26.	Sinthammal	33520	68	F	2.0	0.3	1.7	4.0	CCF
27.	Patchaikani	35385	55	M	2.4	0.8	1.6	1.2	Cirrhosis
28.	Karuppasamy	32791	62	M	2.2	0.5	1.7	2.0	Cirrhosis
29.	Palpandi	32852	35	M	2.7	0.9	1.8	2.0	Liver metastasis
30.	Subramanian	32950	52	M	3.0	2.0	1.0	2.4	TB ascites
31.	Marimuthu	35722	48	M	3.5	1.4	2.1	2.3	Cirrhosis
32.	Sivanammal	37388	54	F	3.0	1.4	1.6	2.0	CCF
33.	Sankarapandi	37412	65	M	2.4	0.5	1.9	0.7	Cirrhosis
34.	Jothi	37225	32	F	3.0	1.2	1.8	2.0	Cirrhosis
35.	Chandhramohan	37136	47	M	2.3	0.5	1.8	4.7	Cirrhosis
36.	Palanisamy	37103	65	M	3.3	0.4	2.9	0.6	Cirrhosis
37.	Muthulakshmi	40743	15	F	3.6	2.7	0.9	6.2	TB ascites
38.	Subbulakshmi	40834	43	F	2.0	0.8	1.2	1.9	CCF
39.	Chelladurai	37685	37	M	3.0	1.8	1.2	4.0	Cirrhosis
40.	Sumathy	40829	30	F	3.9	2.9	1.0	4.0	TB Ascites
41.	Arumugathammal	37702	63	F	3.1	1.0	2.1	3.1	Cirrhosis
42.	Sivanammal	37388	54	F	3.0	2.6	0.4	3.1	TB Ascites
43.	Esakkimuthu	42252	67	M	3.6	2.0	1.6	3.7	Cirrhosis
44.	Chelladurai	43170	52	M	3.0	1.3	1.7	2.3	Cirrhosis
45.	Esakkiammal	42054	45	F	3.0	2.0	1.0	3.4	Peritoneal Carcinomatosis
46.	Annammal	43268	68	F	3.5	2.0	1.5	4.5	Hypothyroidism
47.	Gomathy	43163	65	F	3.2	1.8	1.4	2.2	Cirrhosis
48.	Krishnapriya	41899	24	F	3.0	2.0	1.0	3.1	Pancreatitis
49.	Jothilakshmi	42863	25	F	3.7	2.5	1.2	6.4	CCF
50.	Chellapandi	43281	45	M	3.8	2.5	1.3	2.4	Cirrhosis